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| 10/501,077 | 07/09/2004 | Roland Kellner | MERCK-2907 | 3266 |

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| 23599 | 7590 | 07/18/2007 |
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| EXAMINER | |
| MARTIN, PAUL C | |

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| ART UNIT | PAPER NUMBER |
| 1657 | |

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| 07/18/2007 | PAPER |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/501,077

Applicant(s)

KELLNER ET AL.

Examiner

Paul C. Martin

Art Unit

1657

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 May 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) 6 and 7 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 18 is/are allowed.
- 6) ☒ Claim(s) 1-5, 8, 9 and 11-16 is/are rejected.
- 7) ☒ Claim(s) 10 and 17 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 09 July 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Claims 1-18 are pending in this application, Claims 6 and 7 are withdrawn as being directed toward non-elected inventions, Claims 1-5 and 8-18 were examined on their merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 1-3, 5, 8, 9 and 11-16 remain rejected under 35 U.S.C. § 112, 1st paragraph as failing to comply with the enablement and written description requirement for reasons of record set forth in the Action mailed 01/31/07.

Claims 1-4, 11, 13 and 15 remain rejected under 35 U.S.C. § 112, 2nd paragraph as being indefinite for failing to point out and distinctly claim the subject matter which the applicant regards as the invention for reasons of record set forth in the Action mailed 01/31/07.

Claim Rejections - 35 USC § 102

The rejection of Claims 1-3, 5, 8, 9 and 11-16 remain rejected under 35 U.S.C. § 102(b) as being anticipated by Mountfort *et al.* (1999) as evidenced by Kim *et al.* (1993) for reasons of record set forth in the Action mailed 01/31/07.

Response to Arguments

Applicant's arguments filed 05/02/07 have been fully considered but they are not persuasive.

The Applicant argues that there is insufficient evidence presented to support the allegation that "histidine phosphoamidase, including PHP1 will only hydrolyze P-N bonds and that because the cited references do not disclose the specific examples they cannot be viewed as analogous to the claimed invention (Remarks, Pg. 6, Lines 16-22 and Pg. 7, Lines 1-12), that the specification provides adequate written description of the term "protein histidine-phosphoamidase" and candidate proteins which may constitute proteins that are capable of hydrolyzing phosphorylated basic amino acid residues such as P-His, P-Tyr or P-Arg within peptides or proteins, a representative example of the claimed protein histidine phosphoamidase being PHP1 (Remarks, Pg. 7, Lines 13-21), and that the specification provides adequate written description of phosphoamidase enzymes, substrates, reagents, assay conditions and methods for assaying the activity thereof (Pg. 7, Lines 14-23 and Pg. 8, Lines 1-8).

It is noted that the Applicant appears to be combining arguments to the rejection under 112, 1st enablement and 112, 1st written description as the cited references were only used in support of the rejection under 112, 1st written description. In any event, this is not found to be persuasive for the following reasons, as stated in the prior Action the instant specification specifically defines:

1) a protein phosphoamidase as specific for hydrolyzing N-P histidine residues in peptides or proteins having **no** activity that hydrolyzes O-P peptides or proteins *exemplified* by PHP1;

2) a phosphoamidase as an enzyme hydrolyzing P-N bonds of phosphorylated proteins such as P-His, P-Lys, P-Arg or of peptides or proteins comprising these phosphorylated amino acids and which is devoid of an activity that hydrolyzes O-P proteins or peptides as *exemplified* by the phosphoamidase of Hiraishi *et al.* and PHP1;

3) a protein phosphoamidase as a phosphoamidase hydrolyzing phosphoamide (P-N) bonds of phosphorylated basic proteins such as P-His, P-Lys, P-Arg or of peptides or proteins comprising these phosphorylated amino acids and which is devoid of an activity that hydrolyzes O-P peptides or proteins, *exemplified* by PHP1; and

4) a protein histidine phosphoamidase as a protein phosphoamidase specific for hydrolyzing P-N bonds within peptides or proteins *exemplified* by PHP1.

Moreover, the cited prior art supports the Applicant's own teachings and guidance that phosphoamidase, protein phosphoamidase, and protein histidine phosphoamidase will only hydrolyze P-N bonds and are devoid of the activity of hydrolyzing P-O bonds, therefore in light of the preponderance of teachings and guidance in the specification and the prior art one of ordinary skill in the art would have no motivation or expectation of success of detecting, characterizing and qualitative or quantitatively determining the activity of any phosphoamidase, protein phosphoamidase, and protein histidine phosphoamidase which relies upon the hydrolysis of substrates all containing P-O bonds. However, as noted in the prior action, the instant examples and disclosure taught that PHP1 unexpectedly did hydrolyze certain P-O bonds. Therefore, one of ordinary skill in the art would have been taught or guided to make and/or use the instant invention to detect, characterize and qualitatively or quantitatively determine the activity of PHP1 only based upon the hydrolysis of P-O bond containing substrates. The Applicant has not provided any teachings, guidance or suggestion of any other phosphoamidase, protein phosphoamidase, and protein histidine phosphoamidase which possesses the heretofore unknown activity of hydrolyzing P-O bonds beyond the single example (PHP1) in the disclosure. Therefore, the Applicant has also failed to provide adequate written description for the genus of claims and does not reasonable convey to one of skill in the art that the inventor had possession of the entire scope of the claimed invention.

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The Applicant argues that the cited references of Mountfort *et al.* and Kim *et al.* are drawn to the detection of hydrolysis of P-O bonds by various phosphatase enzymes, and that the Kim *et al.* reference does not assay for the phosphoamidase activity nor employ any of the claimed substrates, and that the skilled artisan would not have envisioned that a substrate with P-O bonds would be suitable for the detection of P-N hydrolyzing enzymes such as phosphoamidases, the skilled artisan would assume that a phosphoamidase enzyme would not be able to hydrolyze P-O containing substrates (Remarks, Pg. 8, Lines 17-29 and Pg. 9. Line1).

This is not found to be persuasive for the following reasons, Mountfort *et al.* teaches an assay method for the identification of an inhibitor of PHP2a using the P-O bond containing substrate FDP, as evidenced by Kim *et al.* PHP2a also has known phosphoamidase P-N bond hydrolyzing activity and therefore the method of Mountfort *et al.* inherently detects the activity of an enzyme with both phosphoester and phosphoamide hydrolyzing activity (PHP2a) and therefore meets the limitations of the claims when given their broadest, reasonable interpretation.

Allowable Subject Matter

Claims 10 and 17 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Claim 18 is free of the art and is allowed, Claims 10 and 17 are objected to, Claims 1-5, 8, 9 and 11-16 remain rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul C. Martin whose telephone number is 571-272-3348. The examiner can normally be reached on M-F 8am-4:30pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Paul Martin
Examiner
Art Unit 1657

07/16/07
/Patricia Leith/
Patricia Leith
Primary Examiner
Art Unit 1655